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EDITORIAL COMMENT

Primary Atherosclerotic Cardiovascular Disease Prevention

Optimally Active, Agile, and Accountable*

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Atherosclerotic cardiovascular disease (ASCVD) affects 24 million adults (1 in every 10) in the United States.[1,2] Low-density lipoprotein cholesterol (LDL-C) is a main causal risk factor for ASCVD, such that there is an estimated 22% relative risk reduction of ASCVD events for every 39 mg/dL LDL-C lowering with statin therapy.[3] Statins remain the foundation of ASCVD prevention and likely confer pleiotropic effects beyond lipid-lowering.[4] Nonetheless, challenges remain with respect to the optimal implementation of guideline-directed approaches to statin initiation.[5]

The 2018 Guideline on the Management of Blood Cholesterol provides a Class I recommendation for the initiation of statin therapy for primary prevention in adults aged 40 to 75 years with type 2 diabetes or LDL-C ≥190 mg/dL as well as those with an intermediate risk (7.5-20%), or high risk (≥20%) based on the Pooled Cohort Equations (PCE) risk calculator.[6] Among select adults with a borderline risk (5-7.5%) or all adults with an intermediate risk (7.5%-20%), there is a Class IIa recommendation to measure coronary artery calcium (CAC) to facilitate clinician-patient risk discussions regarding consideration of statin therapy for primary prevention.[6,7] Measurement of CAC has been shown to help reclassify risk and better identify those most likely to derive net clinical benefit from statin therapy, as the 10-year number needed to treat to prevent 1 ASCVD event is more than 2-fold lower for statin-eligible candidates with incident CAC vs long-term absence of CAC.[8]

The CorCal (Effectiveness of a Proactive Cardiovascular Primary Prevention Strategy, With or Without the Use of Coronary Calcium Screening, in Preventing Future Major Adverse Cardiac Events) trial was an investigator-initiated study conducted in the Intermountain Health system to: 1) compare 2 primary risk assessment strategies for statin selection (based on PCE or CAC scoring); and 2) compare an active approach (ie, using either of these 2 strategies) to a passive approach to statin prescription (usual care).[9] The current study by Anderson et al[10] summarizes the results of the second overarching objective. The CorCal trial enrolled participants aged 50 to 85 in the Intermountain Health system who were identified to be at-risk for ASCVD as determined from review of electronic medical records. A random sample of 3,770 patients were invited by mail, of which 601 gave informed consent (considered to be the active group to receive statin therapy guided by PCE or CAC scoring) and were compared to the group who were invited but did not respond/did not consent (n = 3,169, considered to be the passive group). The investigators noted that the active and passive group were comparable in the baseline characteristics except for a higher prevalence of smoking in the passive arm (14.5% vs 11%). Over a median follow-up of 2.85 years, 25% of the active group were taking statins compared with 10% of the passive group. The active group also had a higher number of lipid panel checks with lower total cholesterol and LDL-C values at the end of the follow-up period (187 mg/dL vs 197 mg/dL; 109 mg/dL vs 117 mg/dL). There were no

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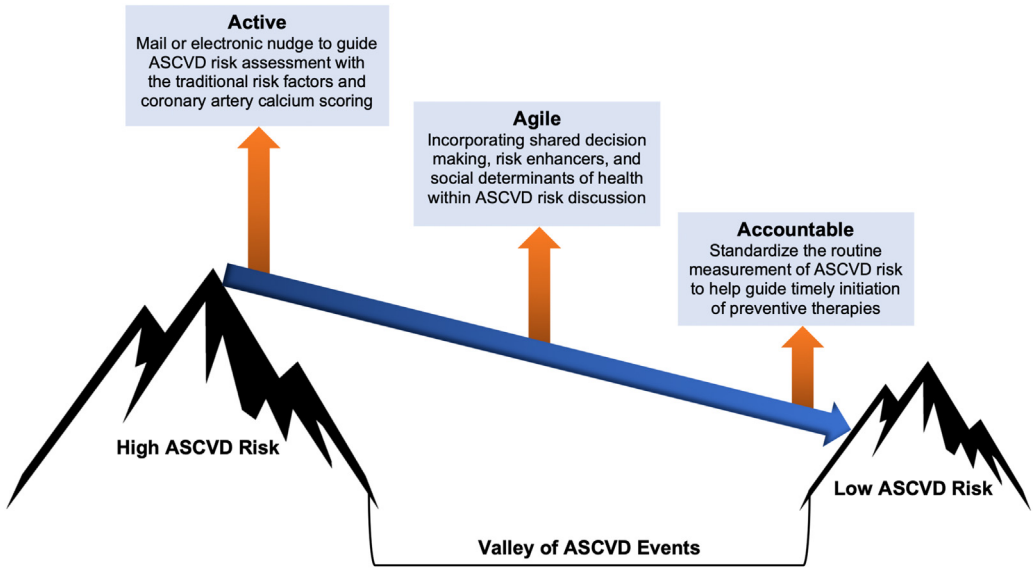
FIGURE 1 Active, Agile, and Accountable Approach to ASCVD Risk Assessment and Prevention



differences in other lipid parameters or ASCVD events between the 2 groups.

Anderson et al should be congratulated for their recent study, which will enrich evidence that supports the utilization of community- and electronic medical record-based efforts for the implementation of evidence-based pharmacotherapy for primary ASCVD prevention. Prospective follow-up and a guideline-centered approach for statin initiation are the main strengths of the current study. Additionally, the CorCal investigational protocol is relatively novel, as the sequence of 10-year ASCVD risk calculation and CAC scoring was synergistic as opposed to algorithmic. Current guidelines provide a Class I recommendation for the routine calculation of 10-year risk with the PCE risk estimator followed by identification of risk enhancing factors for adults aged 40 to 75 years[11] and do not recommend the utilization of CAC scanning unless the calculated 10-year risk is between 5% to 20%. However, select adults may still benefit from measurement of CAC to help guide statin eligibility and initiation.[12]

We acknowledge and agree with the main limitations brought forth by the authors, including an observational study design (no randomization between statin arms), a lack of diversity in the sample (>95% White), and a short duration of median follow-up (<3 years). These 3 latter limitations make the results prone to residual confounding, prevent larger generalizability, and create statistical power concerns. For example, the authors did not perform multivariable modeling to estimate relative risks for: 1) independent variables associated with an active vs passive statin initiation approach; and/or 2) active vs passive statin initiation and the incidence ASCVD events.

Patients included in the current investigation importantly had an established relationship with their physician, which supports the core concept of shared decision-making.[11,13] Implementation of primary prevention pharmacotherapies may be improved upon by broadening patient reach. Recent work has shown that implementation of a standardized remote hypercholesterolemia management program including education and medication titration is associated with higher magnitude reductions in LDL-cholesterol when compared to education alone.[14] Integration of remote management may be helpful in the setting of the CorCal trial given the large percentage of individuals (84%) in the passive study group declined or did not respond to the letter of invitation. Remote monitoring[15] may improve understanding the systems-related challenges, in addition to barriers underlying the high proportion of individuals who did not participate in the active statin initiation group. While the authors did not comment on this finding in the discussion, concerns related to trust in the medical system, impact of social determinants of health, and variable health care literacy may be contributory factors.[16] Affordability of

medications in this study should not be a major barrier preventing the initiation of statins given the widespread availability of generic options.

An approach to primary ASCVD prevention should optimally be active, agile, and accountable (**Figure 1**). An active strategy for the initiation of primary prevention pharmacotherapy, whereas agility is important to incorporate shared decision making and social determinants of health within risk assessment. Finally, accountability and standardization of routine measurement of ASCVD risk is needed to guide timely initiation of preventive therapies. The current study by investigators at Intermountain Health highlights theses 3 As: an active, agile, and accountable approach to help to build the bridge of risk assessment and primary ASCVD prevention.

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